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# The international TREatment of ATopic eczema (TREAT) Registry Taskforce: an initiative to harmonise data collection across national atopic eczema photo- and systemic therapy registries

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## ABBREVIATIONS

AE: Atopic eczema

EMA: European Medicines Agency

ETFAD: European Taskforce for Atopic Dermatitis

FDA: Food and Drug Administration

IEC: International Eczema Council

ISAD: International Society for Atopic Dermatitis

PARENT JA: PAtient REgistries iNiTiative joint action

TREAT: TREatment of ATopic eczema

## KEYWORDS

Atopic eczema, Atopic dermatitis, Patient registries, Immuno-modulatory therapies, Phototherapy

**TO THE EDITOR**

There is an urgent need for novel immuno-modulatory treatments for patients with atopic eczema (AE) (syn. 'atopic dermatitis'); in particular for those with disease recalcitrant to topical therapies. The only conventional systemic therapy approved by the European Medicines Agency (EMA) is cyclosporine; and only in adults. In the US, only oral corticosteroids and dupilumab have Food and Drug Administration (FDA) approval.

At present, the main evidence to inform clinical practice around conventional systemic immuno-modulatory treatments is derived from a rather small body of randomised controlled trials (RCTs) (Roekevisch et al., 2014) as well as case series (i.a. (Garritsen et al., 2015; van der Schaft et al., 2015)). Despite this, in the absence of approved alternatives, immuno-modulatory treatments are frequently prescribed as off-label therapies in children and adults, as shown in our recent European and North American surveys (Proudfoot et al., 2013; Taylor et al., 2016; Totri et al., 2017). Inclusion criteria for clinical trials are stringent; research in psoriasis suggests that around 30% of patients on systemic therapies entered into registries (in itself a very selected subgroup of all patients on systemic therapy) would not be eligible for a clinical trial, underscoring the value of 'real world' patient data (Garcia-Doval et al., 2012).

With the dawn of a new therapeutic era of biologic therapies for AE, some of which have shown great promise in placebo-controlled studies and have been approved by the FDA (Beck et al., 2014; Simpson et al., 2016; Thaci et al., 2016), we need more evidence with regard to effectiveness, safety and cost-effectiveness of such therapies compared to currently used treatment modalities, such as phototherapy and systemic immuno-modulatory drugs (cyclosporine, methotrexate, azathioprine and others).

Apart from the need for comparative real life clinical data of conventional and new therapies, clinical decision-making requires long-term follow-up data on such treatments to generate

information on disease control/disease trajectory modification (even after treatment has been discontinued) and drug safety, including rare adverse events. Generation of reliable data to address these issues requires observation of large patient cohorts for several years. Comprehensive health economic evaluation of these different treatments is routinely required by many national health technology assessment organizations and third party payers to inform the allocation of health care resources. Consequently, independent prospective multi-centre registries are a logical step, as has been successfully developed in psoriasis. This is all the more important in the light of emerging evidence that suggests that industry-funded post-marketing studies, which are often conducted to detect rare adverse events, are not improving drug safety surveillance (Spelsberg et al., 2017).

The international TREatment of ATopic eczema (TREAT) Registry Taskforce (www.comet-initiative.org/studies/details/825?result=true) seeks to find consensus on core domains and domain items for AE research registries and to harmonise data collection on patients receiving systemic immuno-modulatory therapies, following recently published best-practice guidelines of the European Commission funded PAtient REgistries iNiTiative joint action (PARENT JA) (http://patientregistrieseu/guidelines) (Zaletel and Kralj, 2015). PARENT was a collaborating partner of the TREAT Registry Taskforce. This approach will reduce heterogeneity between national registries, enhance interoperability of the national registries, allow direct comparability of individual country data and facilitate data pooling between countries. It will also help to establish compatible data entry platforms.

As a first step on this journey, we recently conducted an international eDelphi exercise and a consensus meeting among 410 dermatologists, nurses, non-clinical researchers involved in AE, pharmaceutical industry representatives, regulatory body representatives and patients from 36 countries, including members of the International Eczema Council (IEC), the European Taskforce for Atopic Dermatitis (ETFAD), and the International Society for Atopic

Dermatitis (ISAD). The study identified a core set of domains and domain items to be captured by national AE patient registries (the 'What' to measure) (Table 1) (Gerbens et al., 2017). Further work is currently underway to define how these domains and domain items should be measured (the 'How' to measure).

We envisage that eligible patients will be children and adults diagnosed with AE who are starting on photo- or systemic immuno-modulatory therapy (conventional immuno-suppressive therapies as well as new biologics), taking into account the national and local eligibility criteria for these specific therapies. Patients receiving intensive topical therapy or screen failures for systemic therapy may also be included. Patients will be followed independently of stopping therapy or subsequent switch to other therapies.

We look forward to working with the global dermatology community on this project, especially those who routinely treat patients with recalcitrant AE; a disease that accounts for more than 20% of total health loss due to skin conditions (Hay et al., 2014) and that has shown a health economic impact similar to that of diabetes mellitus and asthma (Williams et al., 2008). Ultimately, national cohorts of AE patients on photo- and systemic immuno-modulatory therapies will inform treatment guidelines and will also act as a resource for biomarker discovery and pharmacogenetic and pharmacodynamic research. With novel biologic therapies soon to enter our clinical practice, the timing for this project could not be better.

## CONFLICT OF INTEREST

AI has served as a consultant to Anacor, Chugai Pharma, Pfizer, Regeneron, Roche/Genentech, Sanofi-Genzyme and UCB Pharma. CV has advised and given lectures for AbbVie, Chugai, Novartis, Regeneron, Sanofi-Genzyme and UCD Pharma. JS has the lead over the German atopic eczema registry (TREAT Germany) and has received institutional funding for investigator-initiated research from ALK, MSD, Novartis, Pfizer, Sanofi and Wyeth. MD has been a speaker, advisory board member and (principal) investigator for AbbVie, CK-Care Foundation, La Roche Posay Laboratoire Dermatologique, Leo Pharma, Meda Pharma, Pierre Fabre Laboratories, Regeneron, Roche and Sanofi-Genzyme. PS has served as a consultant to AbbVie, Anacor, Leo Pharma and Novartis, has received independent research grants from Leo Pharma and Schering-Plough, and has been involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of AE. SB has received research grants from La Fondation pour la Dermatite Atopique and Pierre Fabre Laboratories, has received personal fees from Bioderma, Ferring, La Roche Posay Laboratoire Dermatologique, Novalac and Sanofi-Genzyme, and has received non-financial support from Abbvie, Janssen and Novartis. SW has served as a consultant to Astellas, Novartis and Sanofi-Genzyme, has received independent research grants from Biogen, Novartis and Pfizer, and has been involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of AE. CF has advised Roche/Genentech and Sanofi/Regeneron. The authors state there are no other conflicts of interests.

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## TABLES

### Table 1. Core set of domains and domain items to be captured in national atopic eczema registries*

| DOMAINS | DOMAIN ITEMS |
|---|---|
| **Demographics** | Date of birth and date of enrolment into registry |
| | Gender |
| | Ethnicity |
| | Educational status |
| | Current occupation or education |
| **AE diagnosis** | How diagnosis AE is established |
| | Use of validated diagnostic criteria |
| | Date of onset AE |
| **Past AE treatments** | Previous phototherapy |
| | Previous systemic therapy |
| | Previous topical treatments for AE |
| | Previous day hospital care treatments for AE (outpatient) |
| | Previous hospitalization for AE |
| **Current AE treatments** | Phototherapy |
| | Systemic immunosuppressive therapy |
| | Topical treatments |
| | Amount of topical creams/ointments used per week |
| **Family history of AE or allergic diseases** | Family history of AE or allergic diseases |
| **Allergic co-morbidities** | Asthma |
| | Allergic rhinoconjunctivitis |
| | Atopic eye disease |
| | Eosinophilic oesophagitis |
| | Food allergies |
| | Contact allergies |
| **Other co-morbidities** | Past malignancies |
| | Past serious infections |
| **Current concomitant medication (i.e. other than specific AE medication** | Antihistamines, oral or topical |
| | Topical antibiotics |
| | Oral antibiotics |
| | Immunosuppressives for other inflammatory diseases |
| **General AE questions** | Exposures that trigger disease flares |
| | Episodes of skin infection (i.e. folliculitis, HSV, molluscum contagiosum) |
| | Days lost from school/college/work |
| **Baseline physical examination** | Fitzpatrick skin type |
| | Skin examination |
| **Baseline physician and patient reported domains** | Physician-assessed clinical signs |
| | Investigator/physician global assessment |
| | Patient-reported symptoms |
| | Patient global assessment |
| | Generic quality of life score |
| | Skin-specific quality of life score |
| | Patient-reported satisfaction with AE care received |
| | Impact of AE on the family |
| **Baseline investigations and assessments** | Medical history (tuberculosis, HIV, hepatitis B or C) |

| | |
|---|---|
| | Full blood count |
| | Liver function |
| | Kidney profile |
| | Evaluating TPMT level prior to azathioprine use |
| **Baseline management** | Reasons for choosing specific treatment (systemic or phototherapy) |
| | Routine recording of relative contraindication(s) for selected treatment |
| **Follow up general AE questions** | Date of death and relation to AE |
| | Change in diagnosis after enrolment (e.g. from AE to CTCL) |
| **Follow up serious adverse events** | Serious adverse events |
| **Follow up adverse events that cause stop or switch of therapy or change in dosage** | Adverse events that cause stop or switch of therapy or change in dosage |
| ***For follow up (serious) adverse events:* probability of relationship with treatment** | *For (serious) adverse events:* probability of relationship with treatment |
| **Follow up physical examination** | Skin examination |
| **Follow up physician and patient reported domains** | Physician-assessed clinical signs |
| | Investigator/physician global assessment |
| | Patient-reported symptoms |
| | Patient global assessment |
| | Generic quality of life score |
| | Skin-specific quality of life score |
| | Reporting of disease control, e.g. flares, fully controlled weeks |
| | Adherence to treatment between appointments |
| | Patient-reported satisfaction with AE care received |
| | Impact of AE on the family |
| **Follow up management** | Reason for switching therapy |
| | Reason for discontinuation of therapy |

Abbreviations: AE, atopic eczema; CTCL, cutaneous T cell lymphoma; HSV, herpes simplex virus; HIV, human immunodeficiency virus, TPMT, thiopurine methyltransferase.

* Results may slightly change after the upcoming 'How' to measure meeting.